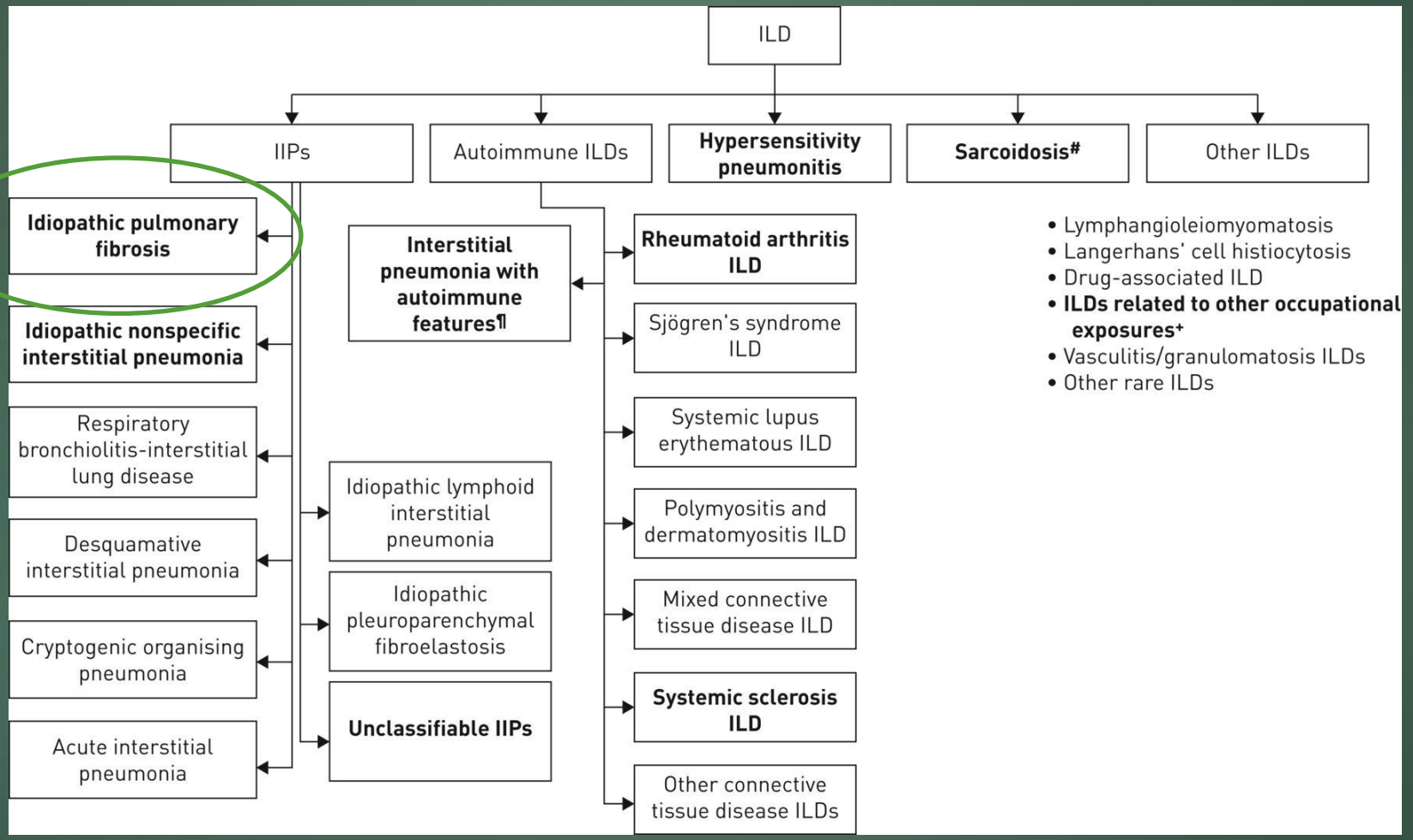
Ιδιοπαθής Πνευμονική Ίνωση Θεραπευτικές επιλογές

Ιφιγένεια Νάκου
Ειδικευόμενη Πνευμονολογίας, Πνευμονολογική Κλινική ΑΠΘ
Γ.Ν. Θ. «Γ. Παπανικολάου», Θεσσαλονίκη

Conflict of interest

- None

Διάχυτες Διάμεσες Πνευμονοπάθειες



Cottin V, Hirani NA, Hotchkin DL, Nambiar AM, Ogura T, Otaola M, Skowasch D, Park JS, Poonyagariyagorn HK, Wuyts W, Wells AU. Presentation, diagnosis and clinical course of the spectrum of progressive-fibrosing interstitial lung diseases. Eur Respir Rev. 2018 Dec 21;27(150):180076. doi: 10.1183/16000617.0076-2018. PMID: 30578335; PMCID: PMC9489068.

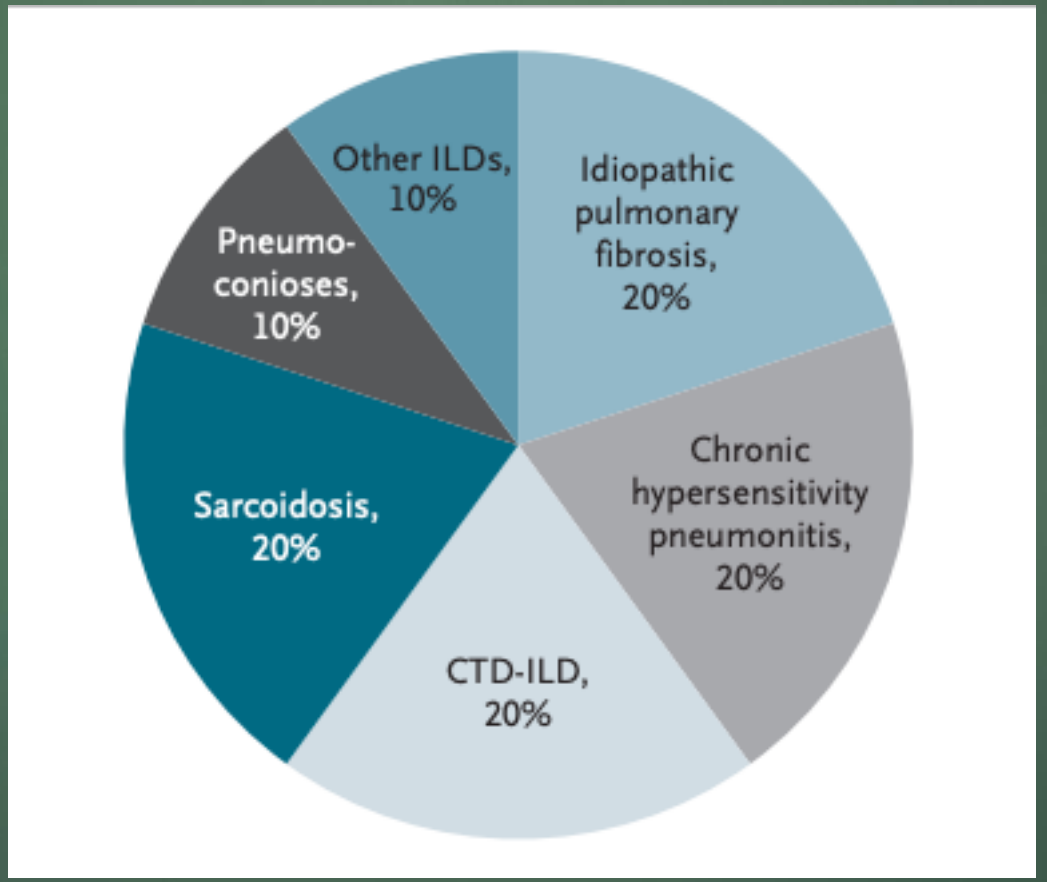
The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Idiopathic Pulmonary Fibrosis

David J. Lederer, M.D., and Fernando J. Martinez, M.D.



AMERICAN THORACIC SOCIETY DOCUMENTS

Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults

An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

Ganesh Raghu, Martine Remy-Jardin, Luca Richeldi, Carey C. Thomson, Yoshikazu Inoue, Takeshi Johkoh, Michael Kreuter, David A. Lynch, Toby M. Maher, Fernando J. Martinez, Maria Molina-Molina, Jeffrey L. Myers, Andrew G. Nicholson, Christopher J. Ryerson, Mary E. Strek, Lauren K. Troy, Marlies Wijsenbeek, Manoj J. Mammen, Tanzib Hossain, Brittany D. Bissell, Derrick D. Herman, Stephanie M. Hon, Fayez Kheir, Yet H. Khor, Madalina Macrea, Katerina M. Antoniou, Demosthenes Bouros, Ivette Buendia-Roldan, Fabian Caro, Bruno Crestani, Lawrence Ho, Julie Morisset, Amy L. Olson, Anna Podolanczuk, Venerino Poletti, Moisés Selman, Thomas Ewing, Stephen Jones, Shandra L. Knight, Marya Ghazipura, and Kevin C. Wilson; on behalf of the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Asociación Latinoamericana de Tórax

This official clinical practice guideline was approved by the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Asociación Latinoamericana de Tórax February 2022

- Χρόνια, ινωτική διάμεση πνευμονοπάθεια
- Άγνωστη αιτιολογία
- Ακτινολογικά και ιστολογικά χαρακτηριστικά UIP

- Ενήλικες >65 ετών
- Σταδιακά επιδεινούμενη δύσπνοια και αναπνευστική λειτουργία
- Πτωχή πρόγνωση

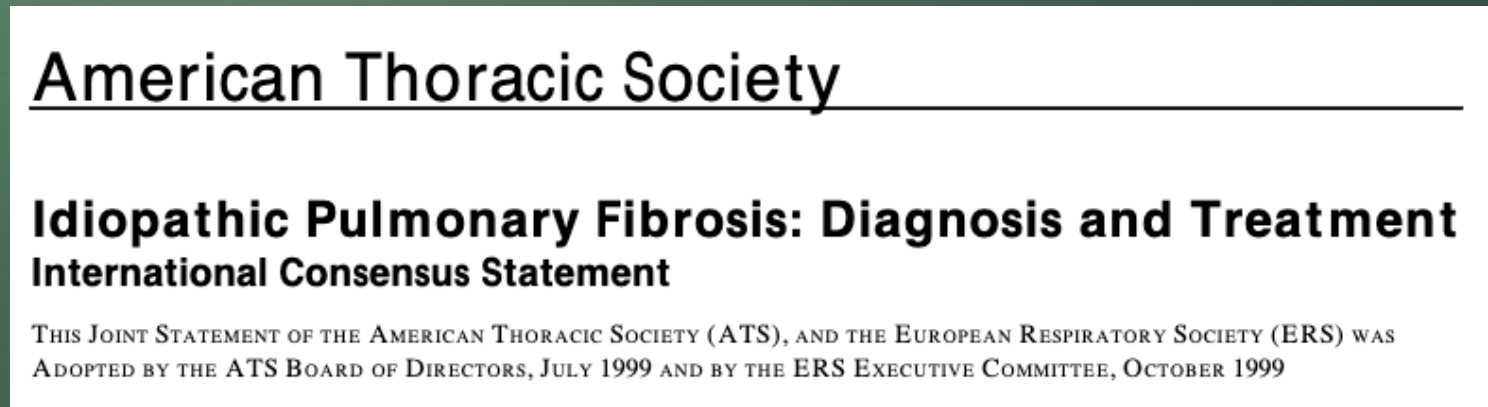
Παράγοντες που επηρεάζουν την επιβίωση σε ασθενείς με IPF

- Ελάττωση της FVC
- Ελάττωση της DLCO
- Οξείες παροξύνσεις
- Συννοσηρότητες
- Επίπεδο βαρύτητας

Θεραπευτικές επιλογές

ΠΡΙΝ ΤΟ 2020

- Κορτικοστεροειδή
- Ανοσοκατασταλτικά – κυτταροτοξικά
  - Αζαθειοπρίνη, κυκλοφωσφαμίδη
- Αντιινωτικοί παράγοντες
  - κολχικίνη



American Thoracic Society

Idiopathic Pulmonary Fibrosis: Diagnosis and Treatment
International Consensus Statement

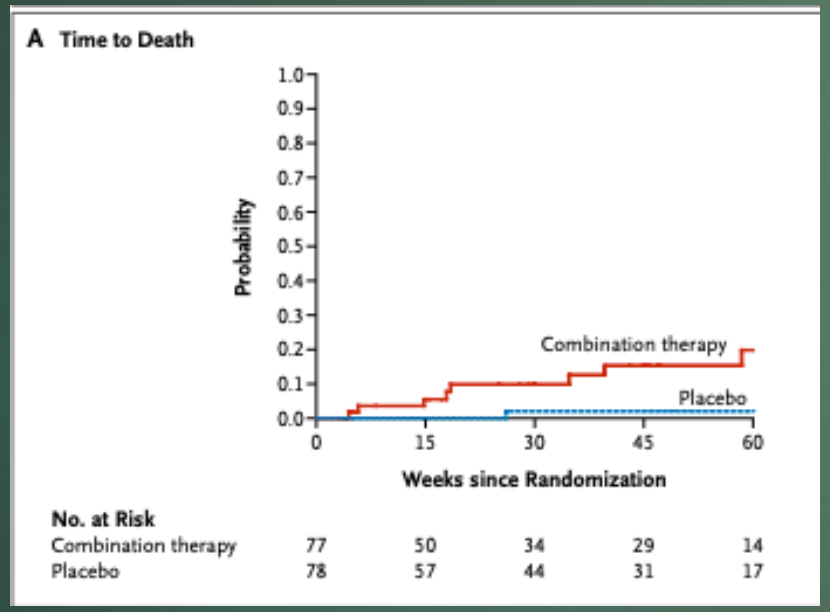
This Joint Statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was Adopted by the ATS Board of Directors, July 1999 and by the ERS Executive Committee, October 1999

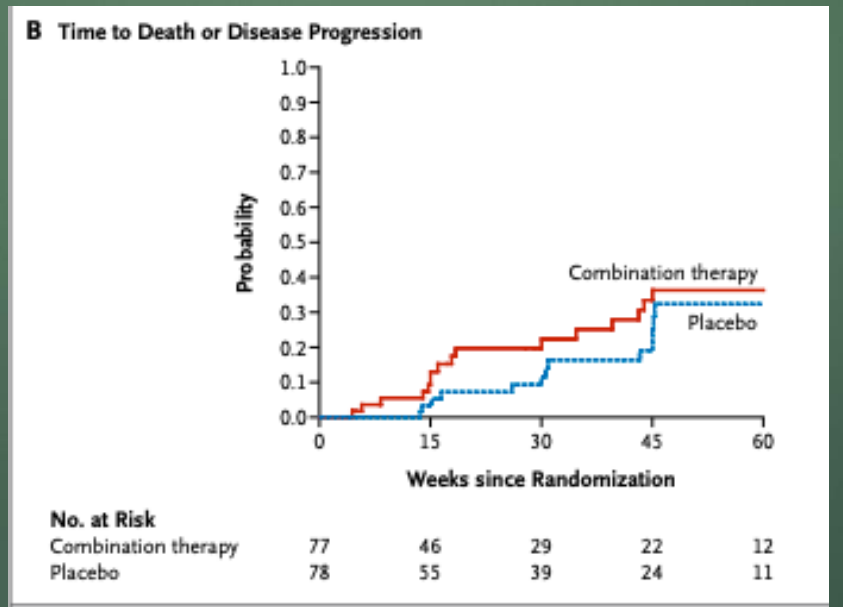
The NEW ENGLAND JOURNAL of MEDICINE

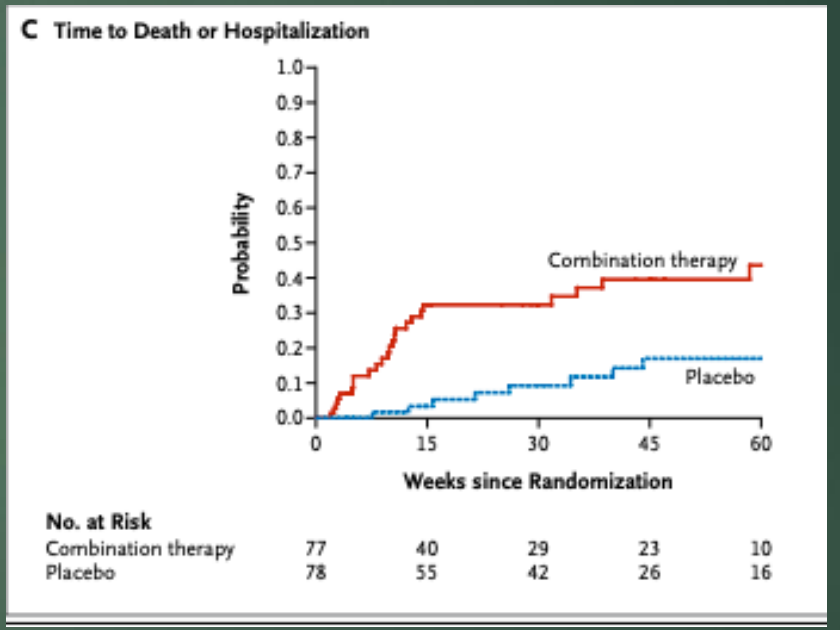
ORIGINAL ARTICLE

Prednisone, Azathioprine, and N-Acetylcysteine for Pulmonary Fibrosis

The Idiopathic Pulmonary Fibrosis Clinical Research Network*







The NEW ENGLAND JOURNAL of MEDICINE

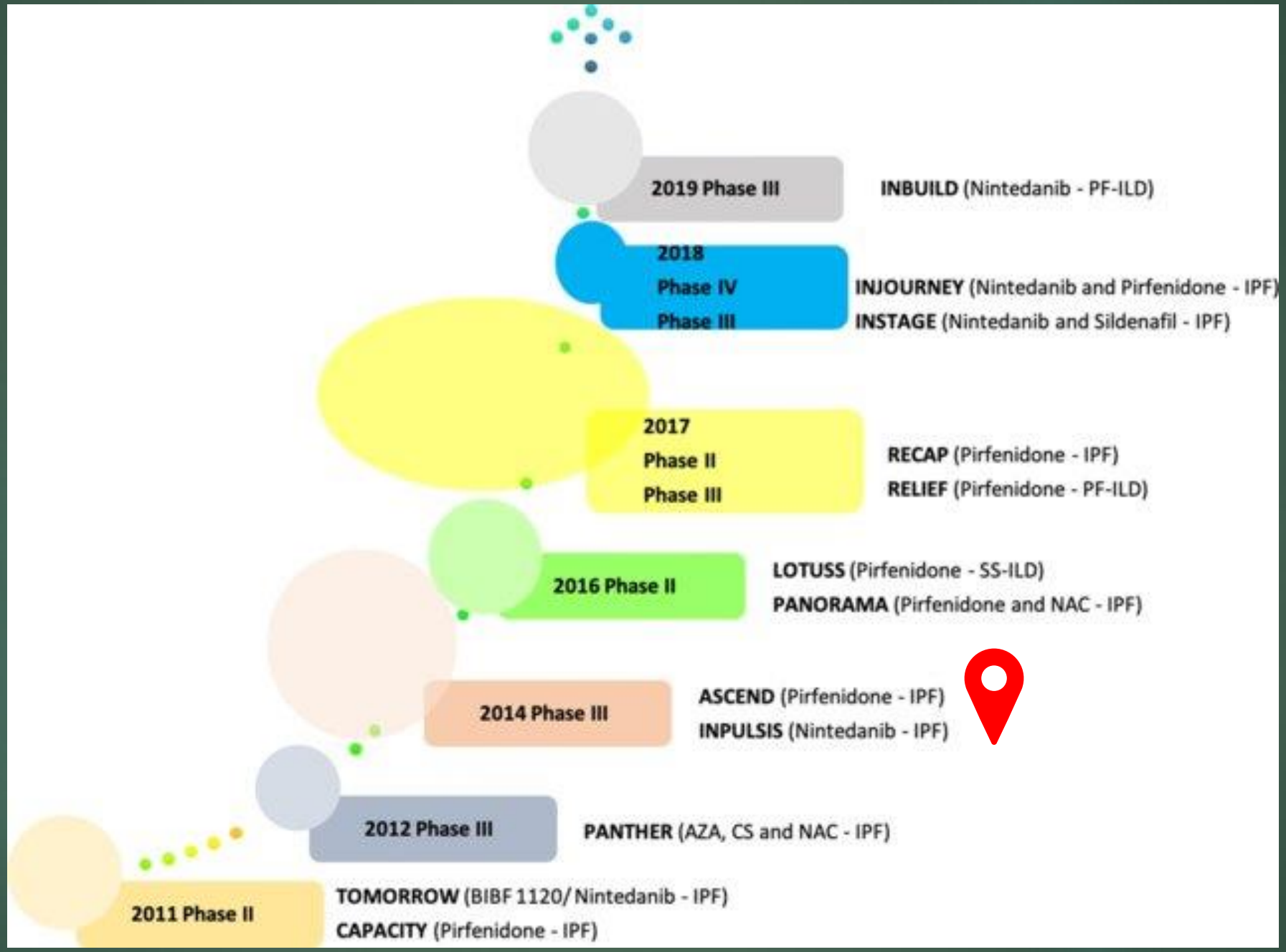
ORIGINAL ARTICLE

Prednisone, Azathioprine, and N-Acetylcysteine for Pulmonary Fibrosis

The Idiopathic Pulmonary Fibrosis Clinical Research Network*

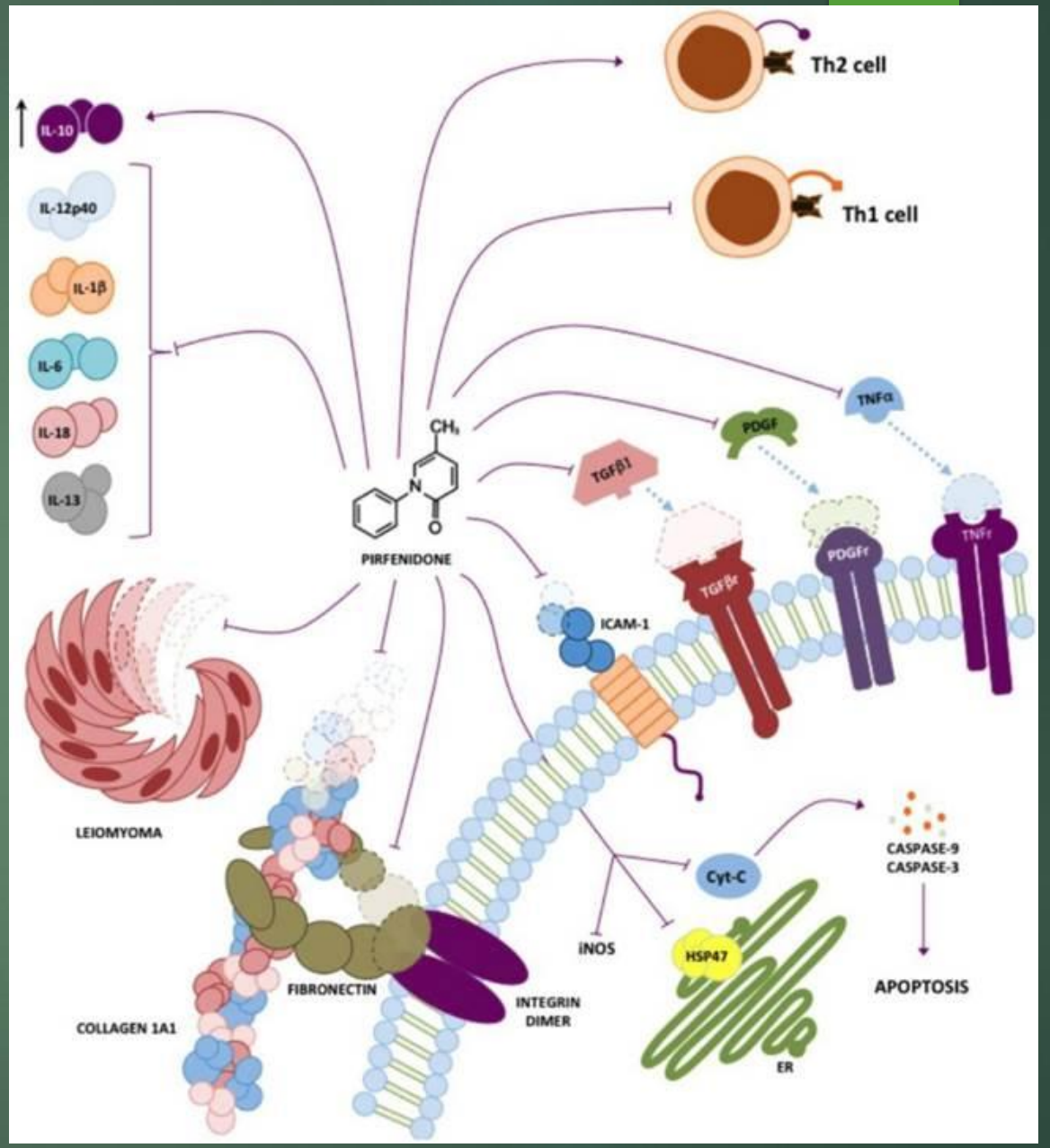
CONCLUSIONS

Increased risks of death and hospitalization were observed in patients with idiopathic pulmonary fibrosis who were treated with a combination of prednisone, azathioprine, and NAC, as compared with placebo. These findings provide evidence against the use of this combination in such patients. (Funded by the National Heart, Lung, and Blood Institute and the Cowlin Family Fund; ClinicalTrials.gov number, NCT00650091.)


2019 Phase III
INBUILD (Nintedanib - PF-ILD)
2018
Phase IV
Phase III
INJOURNEY (Nintedanib and Pirfenidone - IPF)
INSTAGE (Nintedanib and Sildenafil - IPF)
2017
Phase II
Phase III
RECAP (Pirfenidone - IPF)
RELIEF (Pirfenidone - PF-ILD)
2016 Phase II
LOTUSS (Pirfenidone - SS-ILD)
PANORAMA (Pirfenidone and NAC - IPF)
2014 Phase III
ASCEND (Pirfenidone - IPF)
INPULSIS (Nintedanib - IPF)
2012 Phase III
PANTHER (AZA, CS and NAC - IPF)
2011 Phase II
TOMORROW (BIBF 1120/ Nintedanib - IPF)
CAPACITY (Pirfenidone - IPF)

Pirfenidone

- Αντι-ινωτικό
- Μειώνει τον πολλαπλασιασμό των ινοβλαστών και την εναπόθεση κολλαγόνου

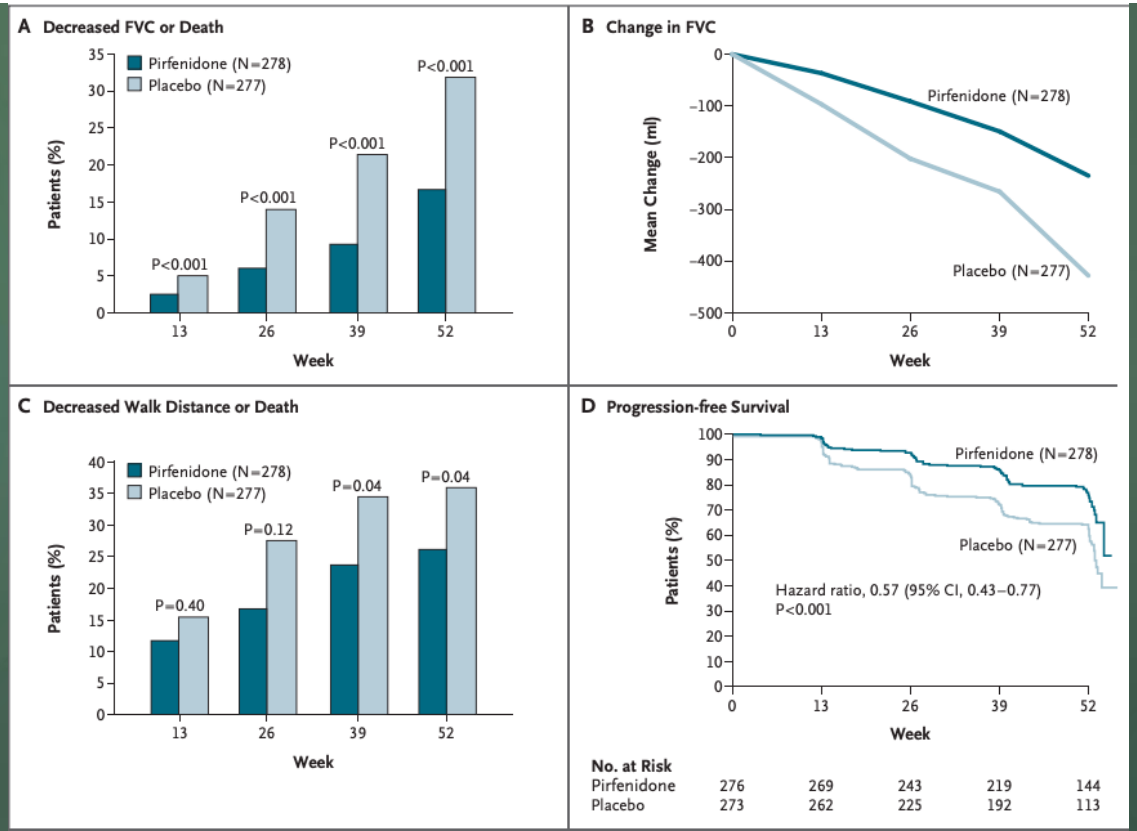


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Phase 3 Trial of Pirfenidone in Patients with Idiopathic Pulmonary Fibrosis

Talmadge E. King, Jr., M.D., Williamson Z. Bradford, M.D., Ph.D., Socorro Castro-Bernardini, M.D., Elizabeth A. Fagan, M.D., Ian Glaspole, M.B., B.S., Ph.D., Marilyn K. Glassberg, M.D., Eduard Gorina, M.D., Peter M. Hopkins, M.D., David Kardatzke, Ph.D., Lisa Lancaster, M.D., David J. Lederer, M.D., Steven D. Nathan, M.D., Carlos A. Pereira, M.D., Steven A. Sahn, M.D., Robert Sussman, M.D., Jeffrey J. Swigris, D.O., and Paul W. Noble, M.D., for the ASCEND Study Group*



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CONCLUSIONS

Pirfenidone, as compared with placebo, reduced disease progression, as reflected by lung function, exercise tolerance, and progression-free survival, in patients with idiopathic pulmonary fibrosis. Treatment was associated with an acceptable side-effect profile and fewer deaths. (Funded by InterMune; ASCEND ClinicalTrials.gov number, NCT01366209.)

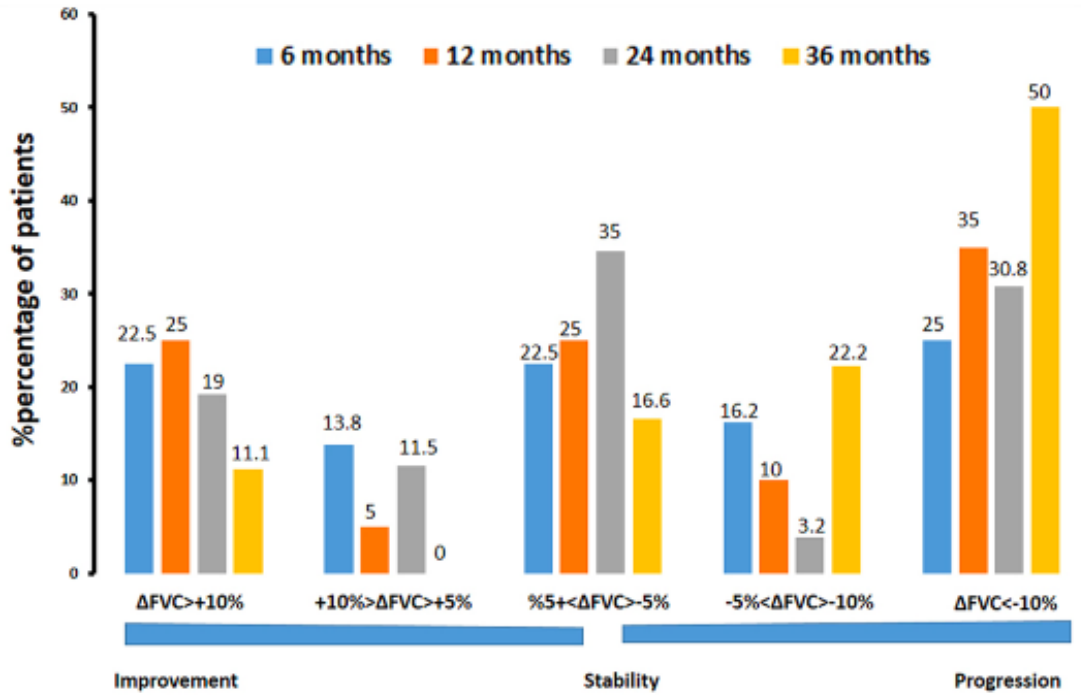
frontiers in Medicine

ORIGINAL RESEARCH
published: 29 November 2017
doi: 10.3389/fmed.2017.00213

Longitudinal "Real-World" Outcomes of Pirfenidone in Idiopathic Pulmonary Fibrosis in Greece

Argyrios Tzouvelekis[1,2†‡], Theodoros Karampitsakos[3†], Paschalis Ntolios[4], Vasilios Tzilas[1], Evangelos Bouros[1], Evangelos Markozannes[1], Ioanna Malliou[1], Aris Anagnostopoulos[1], Andreas Granitsas[1], Paschalis Steiropoulos[2], Katerina Dimakou[3], Serafeim Chrysikos[4], Nikolaos Koulouris[1] and Demosthenes Bouros[1‡]*

[1] First Academic Department of Pneumonology, Hospital for Diseases of the Chest "Sotiria", Medical School, National and Kapodistrian University of Athens, Athens, Greece, [2] Division of Immunology, Biomedical Sciences Research Center "Alexander Fleming", Athens, Greece, [3] 5th Respiratory Department, Hospital for Diseases of the Chest "Sotiria", Athens, Greece, [4] Department of Pneumonology, University Hospital of Alexandroupolis, Democritus University of Thrace, Komotini, Greece



Pirfenidone

- Tabs 801mg 3 φορές ημερησίως

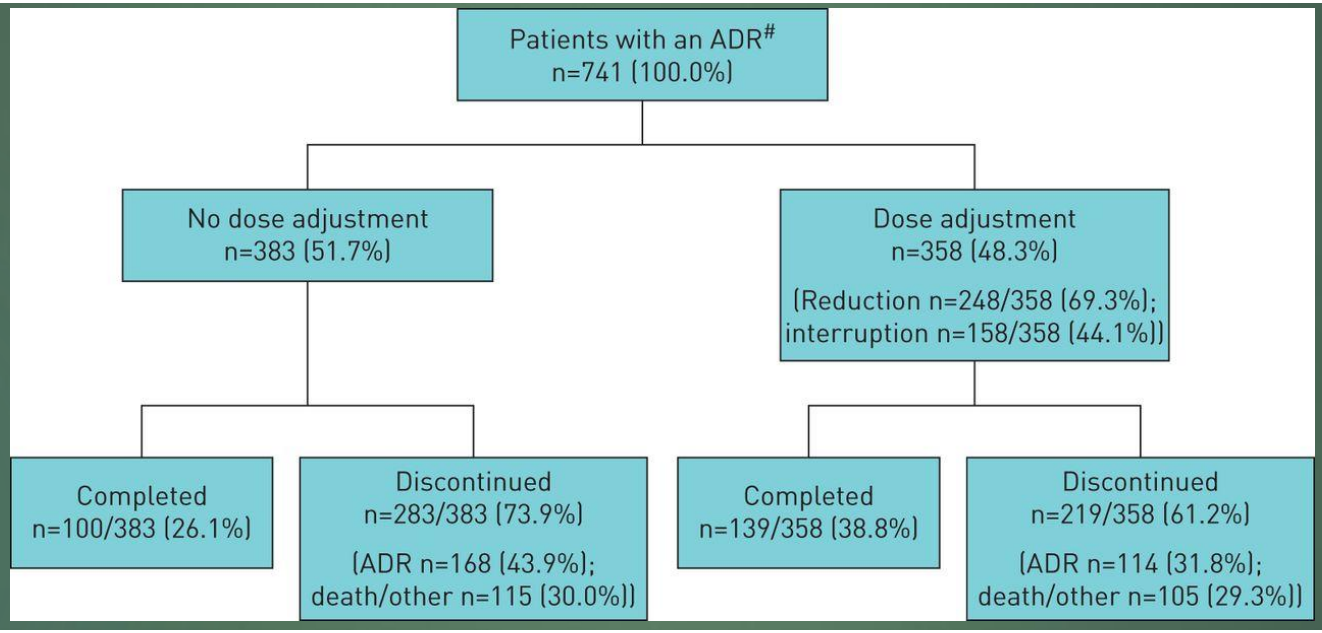
Τιτλοποίηση δόσης σε διάστημα 21 ημερών

- Διαταραχές ΓΕΣ
  - Ναυτία
  - Διάρροια
- Φωτοευαισθησία
- Εξάνθημα

ERJ open research

Long-term safety of pirfenidone: results of the prospective, observational PASSPORT study

Vincent Cottin[1,2], Dirk Koschel[3], Andreas Günther[4,5], Carlo Albera[6], Arata Azuma[7], C. Magnus Sköld[8,9], Sara Tomassetti[10], Philip Hormel[11], John L. Stauffer[11], Indiana Strombom[11], Klaus-Uwe Kirchgaessler[12] and Toby M. Maher[13,14]

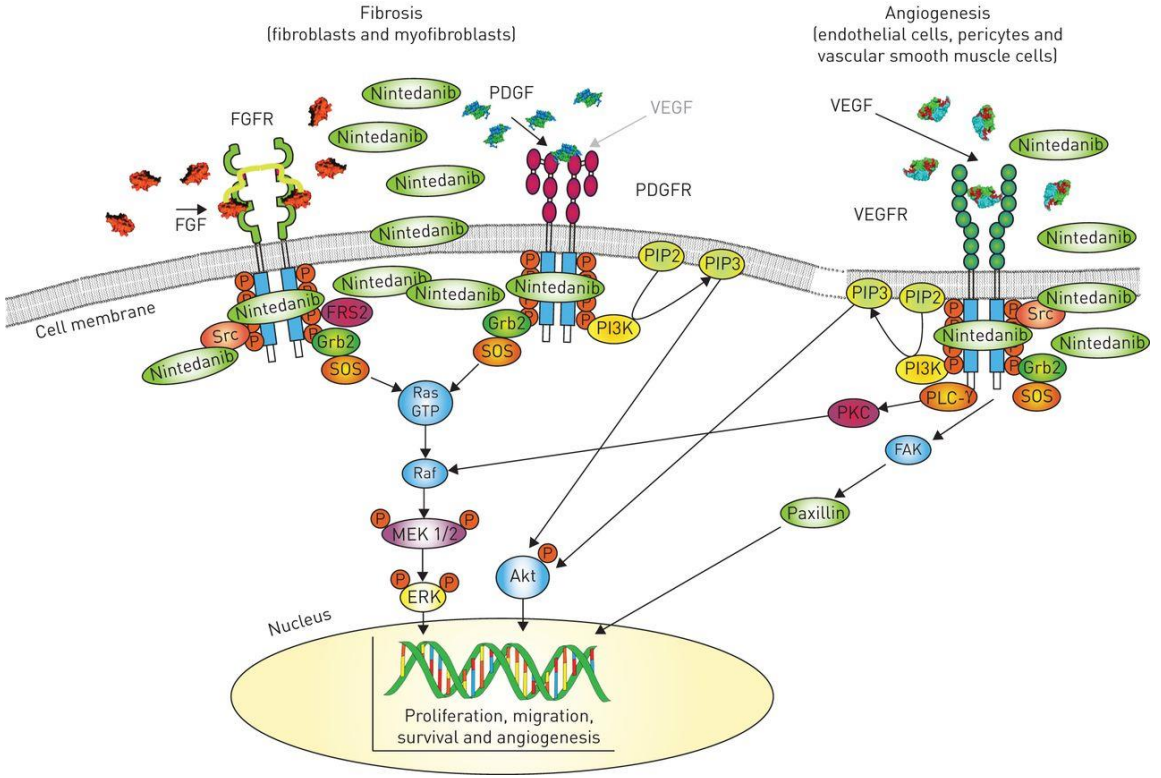


In summary, no new safety signals were observed in PASSPORT when compared with the pirfenidone RCTs and other post-marketing experience. The safety findings in this study are consistent with the established safety profile of pirfenidone. Furthermore, dose adjustment had a favourable effect on treatment persistence. This study also provides new data on the safety findings of patients within pre-defined subgroups that support the established safety profile of pirfenidone. Identification of predictors of early treatment discontinuation due to an ADR, including older age, female sex and prior steroid use, allows better targeting of patient information to help manage ADRs in these patients.

Nintedanib

- Αναστολέας της τυροσινικής κινάσης
- Αναστολή του υποδοχέα του PDGF
- Αναστολή του υποδοχέα FGF
- Αναστολή του υποδοχέα VEGF
- Δεσμεύεται ανταγωνιστικά στη θέση πρόσδεσης της τριφωσφορικής αδενοσίνης (ATP)

Εμποδίζει την ενδοκυτταρική μεταφορά σημάτων που συμμετέχουν στην αναδιαμόρφωση ινωτικού ιστού



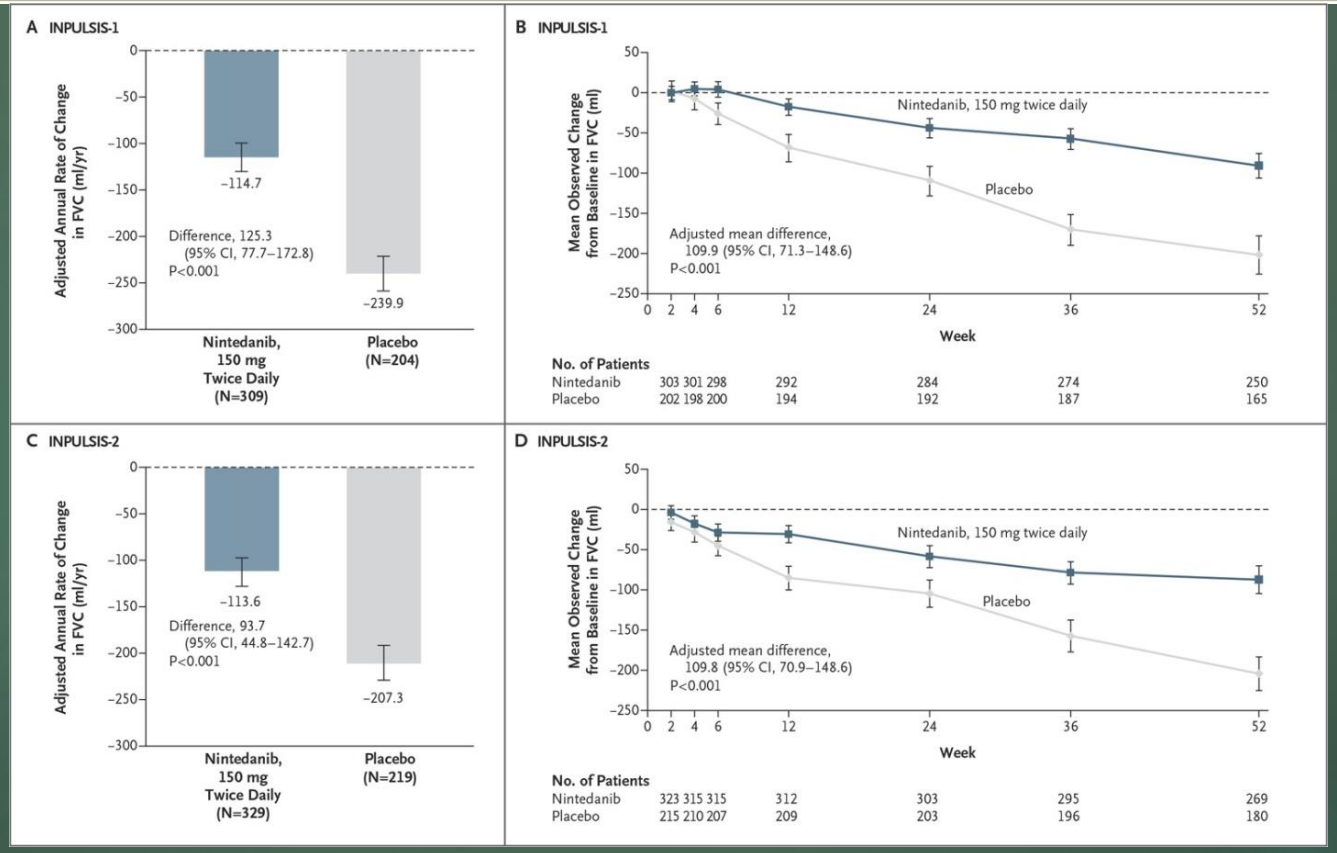
Wollin L, Wex E, Pautsch A, Schnapp G, Hostettler KE, Stowasser S, Kolb M. Mode of action of nintedanib in the treatment of idiopathic pulmonary fibrosis. Eur Respir J. 2015 May;45(5):1434-45.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 29, 2014 VOL. 370 NO. 22

Efficacy and Safety of Nintedanib in Idiopathic Pulmonary Fibrosis

Luca Richeldi, M.D., Ph.D., Roland M. du Bois, M.D., Ganesh Raghu, M.D., Arata Azuma, M.D., Ph.D., Kevin K. Brown, M.D., Ulrich Costabel, M.D., Vincent Cottin, M.D., Ph.D., Kevin R. Flaherty, M.D., David M. Hansell, M.D., Yoshikazu Inoue, M.D., Ph.D., Dong Soon Kim, M.D., Martin Kolb, M.D., Ph.D., Andrew G. Nicholson, D.M., Paul W. Noble, M.D., Moisés Selman, M.D., Hiroyuki Taniguchi, M.D., Ph.D., Michèle Brun, M.Sc., Florence Le Maulf, M.Sc., Mannaïg Girard, M.Sc., Susanne Stowasser, M.D., Rozsa Schlenker-Herceg, M.D., Bernd Disse, M.D., Ph.D., and Harold R. Collard, M.D., for the INPULSIS Trial Investigators*



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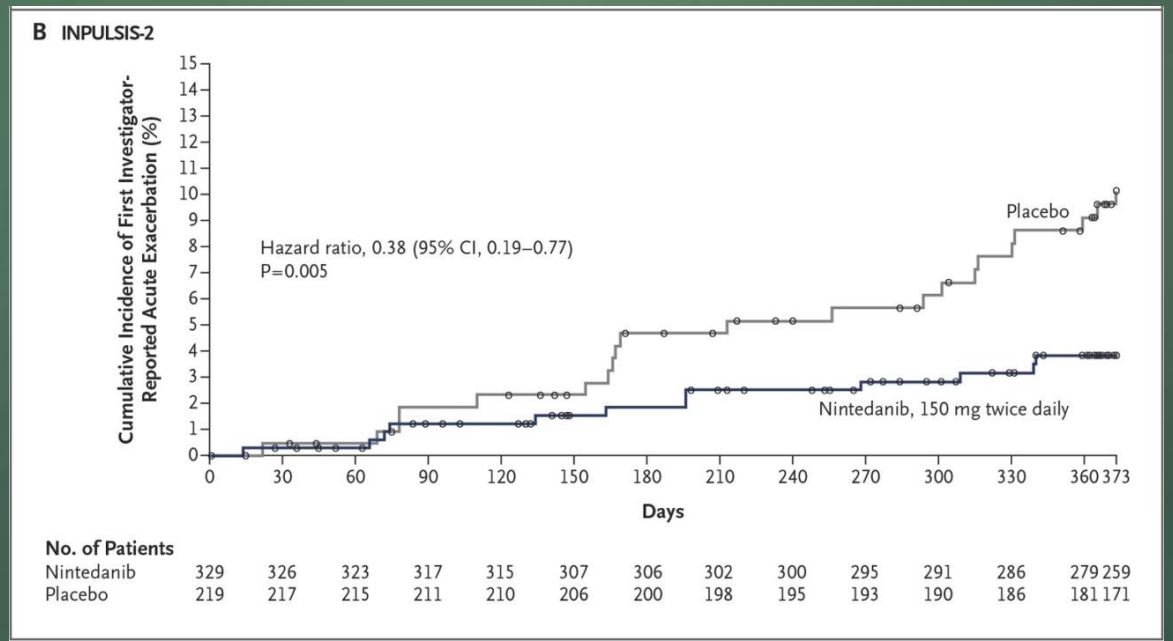


Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Nintedanib in patients with idiopathic pulmonary fibrosis: Combined evidence from the TOMORROW and INPULSIS® trials

Luca Richeldi [a, *], Vincent Cottin [b], Roland M. du Bois [c], Moisés Selman [d], Toshio Kimura [e], Zelie Bailes [f], Rozsa Schlenker-Herceg [g], Susanne Stowasser [e], Kevin K. Brown [h]

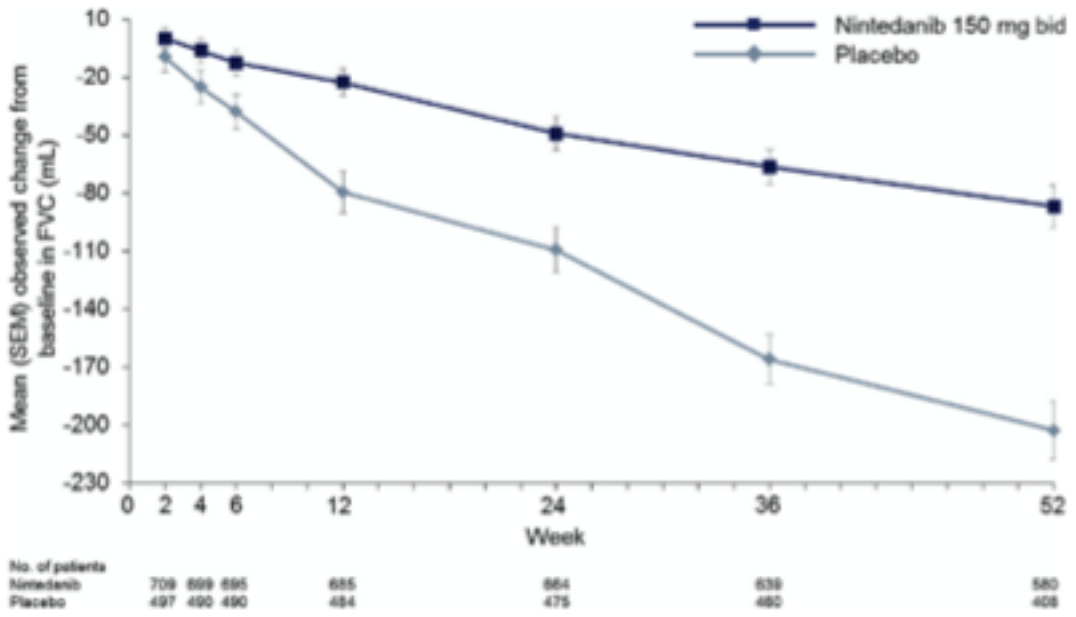


Fig. 2. Changes in FVC over time: pooled data from the TOMORROW and INPULSIS® trials.

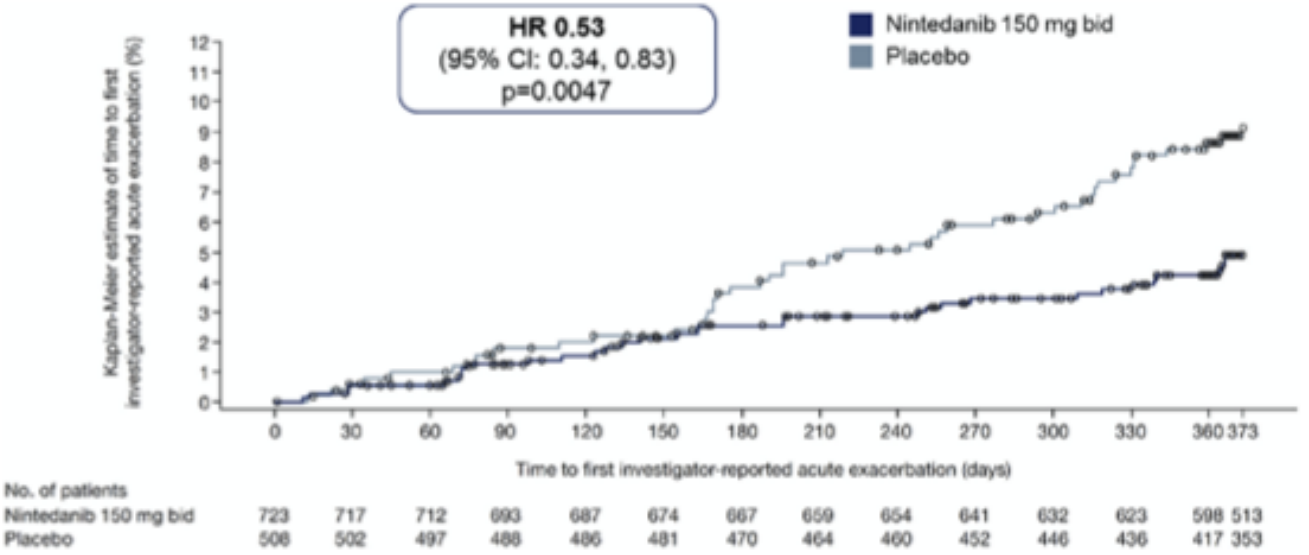


Fig. 3. Time to first investigator-reported acute exacerbation: pooled data from the TOMORROW and INPULSIS® trials.

ERJ open research

Efficacy and safety of nintedanib in a Greek multicentre idiopathic pulmonary fibrosis registry: a retrospective, observational, cohort study

Katerina Antoniou[1,7], Katerina Markopoulou[2,7], Argyrios Tzouvelekis[3,7], Athina Trachalaki[1,7], Eirini Vasarmidi[1,7], Jiannis Organtzis[4,7], Vasilios Tzilas[3], Evangelos Bouros[3], Georgia Kounti[2], Christina Rampiadou[2], Serafeim-Chrysovalantis Kotoulas[2], Fotini Bardaka[5], Eleni Bibaki[6], Evangelia Fouka[4], Georgios Meletis[6], Stavros Tryfon[2], Zoe Daniil[5], Despina Papakosta[4] and Demosthenes Bouros[3]

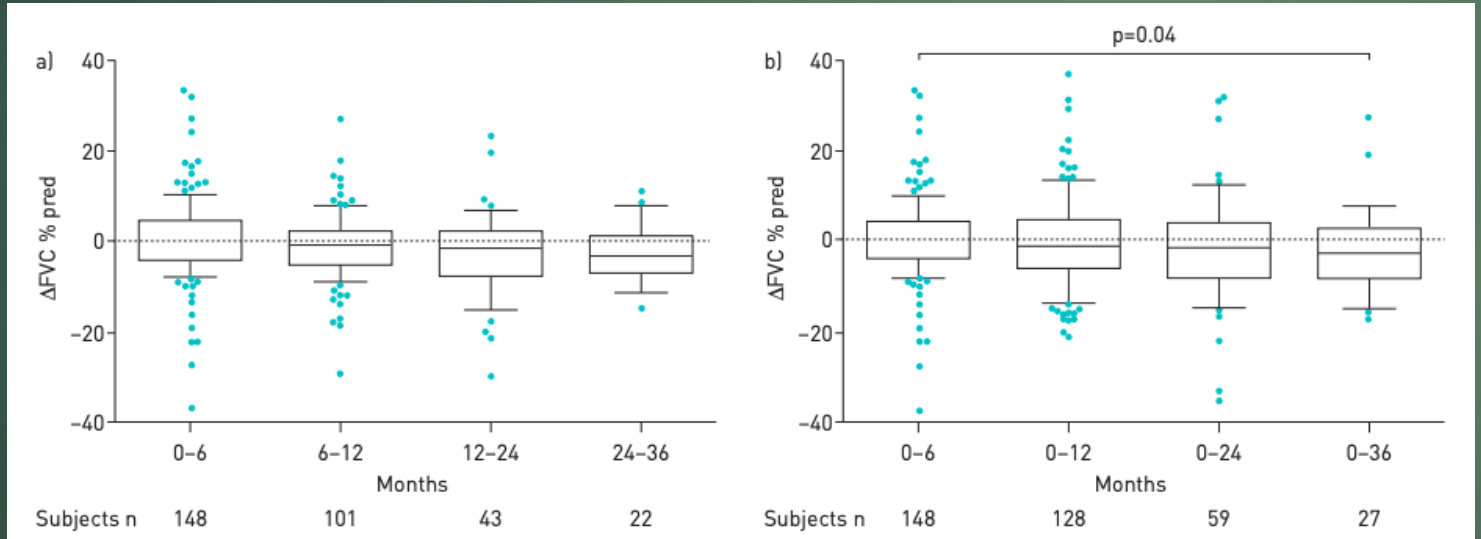


FIGURE 2 a) Change in forced vital capacity (FVC)% predicted at 0–6, 6–12, 12–24 and 24–36 months; b) change from baseline in FVC% pred at 6, 12, 24, and 36 months. Patients were censored from the analysis after death and/or discontinuation.

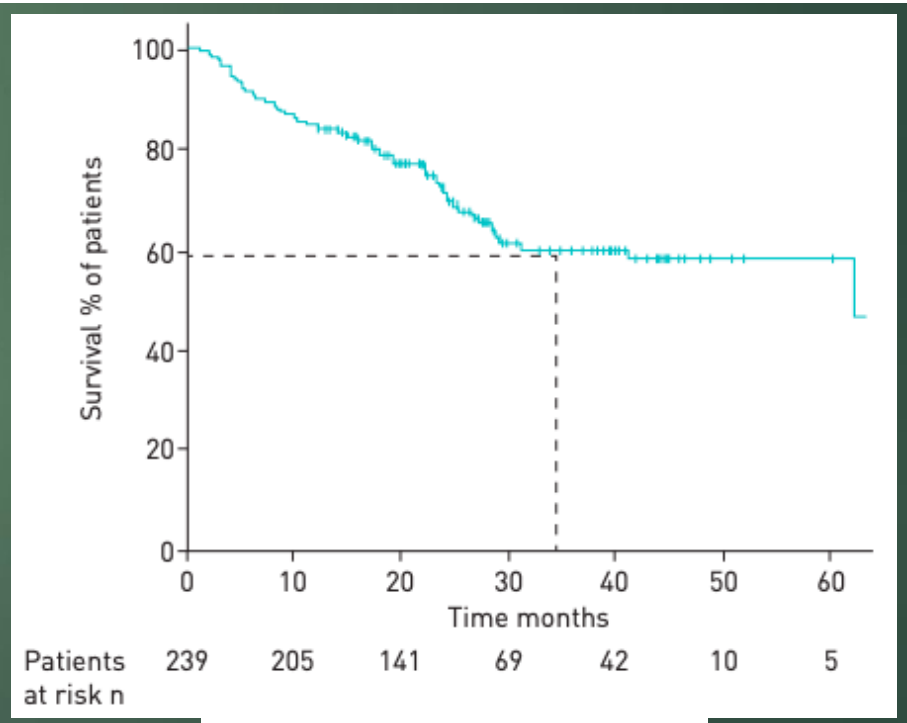


FIGURE 1 Survival after 3 years on nintedanib treatment (n=239), mean±SD survival 54.7±3.5 months.

ERJ open research

Efficacy and safety of nintedanib in a Greek multicentre idiopathic pulmonary fibrosis registry: a retrospective, observational, cohort study

Katerina Antoniou[1,7], Katerina Markopoulou[2,7], Argyrios Tzouvelekis[3,7], Athina Trachalaki[1,7], Eirini Vasarmidi[1,7], Jiannis Organtzis[4,7], Vasilios Tzilas[3], Evangelos Bouros[3], Georgia Kounti[2], Christina Rampiadou[2], Serafeim-Chrysovalantis Kotoulas[2], Fotini Bardaka[5], Eleni Bibaki[6], Evangelia Fouka[4], Georgios Meletis[6], Stavros Tryfon[2], Zoe Daniil[5], Despina Papakosta[4] and Demosthenes Bouros[3]

TABLE 2 Investigator-reported adverse events in the safety population

	Adverse events	Proportion of patients with adverse event %
Total adverse events reported	224	55.7
GI events	173	
Diarrhoea	110	45.0
Nausea/vomiting	26	10.7
Anorexia	18	7.4
Abdominal pain	11	4.5
Dyspepsia/bloating	6	2.5
GI bleeding	2	0.8
Reduced body weight	16	6.6
Liver function test elevations	12	4.9
Weakness	11	4.5
Ischaemic events#	9	2.9
Hyperpyrexia	1	0.4
Others	4	1.6
Reduced dose due to adverse event	69	28.3
Discontinuation due to adverse event	32	13.1

GI: gastrointestinal. #: myocardial infarction or ischaemic stroke.

Nintedanib

- Caps 150mg, 2 φορές ημερησίως

Ή

- Caps 100mg, 2 φορές ημερησίως

- Διαταραχές ΓΕΣ
  - Διάρροια
  - Ναυτία / έμετος
- Αύξηση ηπατικών ενζύμων (ALT, AST, ALP, GGT)
- Αιμορραγία

Respiratory Medicine 159 (2019) 105803

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: http://www.elsevier.com/locate/rmed

Real-life comparison of pirfenidone and nintedanib in patients with idiopathic pulmonary fibrosis: A 24-month assessment

Stefania Cerri [a,1], Matteo Monari [b,1], Aldo Guerrieri [c], Pierluigi Donatelli [d], Ilaria Bassi [b], Martina Garuti [d], Fabrizio Luppi [e], Sara Betti [b], Gianpiero Bandelli [b], Marco Carpano [b], Maria Letizia Bacchi Reggiani [f], Roberto Tonelli [d,g], Enrico Clini [a,b,c,d,2], Stefano Nava [b,*,2]

A B S T R A C T

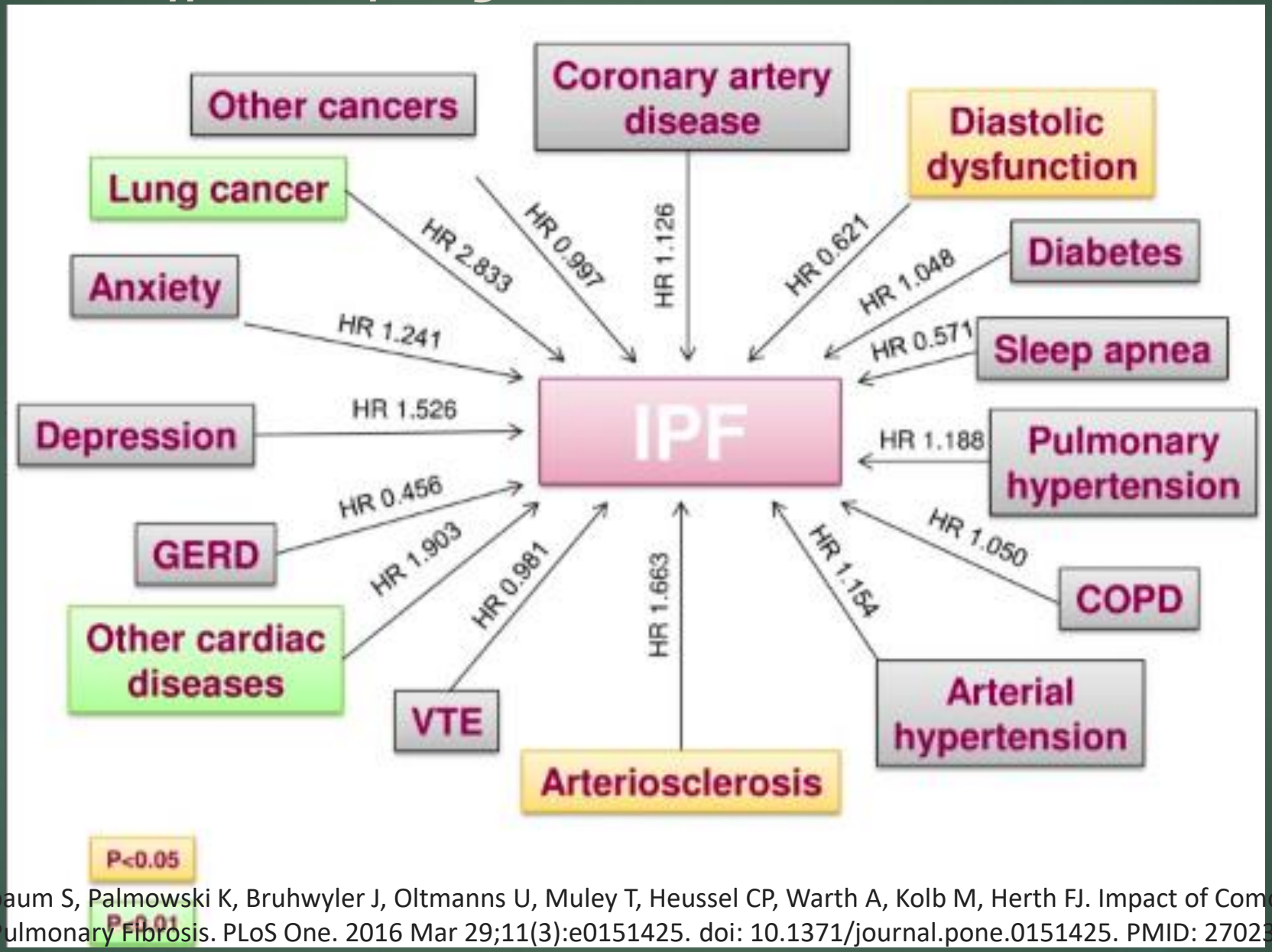
Background: Real-life data on the use of pirfenidone and nintedanib to treat patients with idiopathic pulmonary fibrosis (IPF) are still scarce.

Methods: We compared the efficacy of either pirfenidone (n = 78) or nintedanib (n = 28) delivered over a 24-month period in patients with IPF, followed at two regional clinic centers in Italy, with a group of patients who refused the treatment (n = 36), and who were considered to be controls. All patients completed regular visits at 1- to 3-month intervals, where primary [forced vital capacity (FVC) and diffusing capacity of the lungs for carbon monoxide (DLCO)] and secondary outcomes (side effects, treatment compliance, and mortality) were recorded.

Results: Over time, the decline in FVC and DLCO was significantly higher (p = 0.0053 and p = 0.037, respectively) in controls when compared with the combined treated group, with no significant difference between the two treated groups. Compared to patients with less advanced disease (GAP (Gender, Age, Physiology) stage I), those in GAP stages II and III showed a significantly higher decline in both FVC and DLCO irrespective of the drug taken. Side effects were similarly reported in patients receiving pirfenidone and nintedanib (5% and 7%, respectively), whereas mortality did not differ among the three groups.

Conclusion: This real-life study demonstrated that both pirfenidone and nintedanib were equally effective in reducing the decline of FVC and DLCO versus non-treated patients after 24 months of treatment; however, patients with more advanced disease were likely to show a more rapid decline in respiratory function.

Συννοσηρότητες



Kreuter M, Ehlers-Tenenbaum S, Palmowski K, Bruhwyler J, Oltmanns U, Muley T, Heussel CP, Warth A, Kolb M, Herth FJ. Impact of Comorbidities on Mortality in Patients with Idiopathic Pulmonary Fibrosis. PLoS One. 2016 Mar 29;11(3):e0151425. doi: 10.1371/journal.pone.0151425. PMID: 27023440; PMCID: PMC4811578.

Θεραπεία με αντιόξινα (PPIs)

- ✗ Disease progression: no statistically significant effect
- ✗ Mortality: no significant difference
- ✗ Exacerbations and/or hospitalization: no statistically significant effect
- ✗ Lung function: no difference
- ✓ Adverse Effects: no difference

very low quality of evidence

Raghu G, Remy-Jardin M, Richeldi L, Thomson CC, Inoue Y, Johkoh T, Kreuter M, Lynch DA, Maher TM, Martinez FJ, Molina-Molina M, Myers JL, Nicholson AG, Ryerson CJ, Strek ME, Troy LK, Wijsenbeek M, Mammen MJ, Hossain T, Bissell BD, Herman DD, Hon SM, Kheir F, Khor YH, Macrea M, Antoniou KM, Bouros D, Buendia-Roldan I, Caro F, Crestani B, Ho L, Morisset J, Olson AL, Podolanczuk A, Poletti V, Selman M, Ewing T, Jones S, Knight SL, Ghazipura M, Wilson KC. Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults: An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. Am J Respir Crit Care Med. 2022 May 1;205(9):e18-e47.

Μη φαρμακευτικές επιλογές

- Διακοπή καπνίσματος
- Εμβολιασμοί
- Οξυγονοθεραπεία
- Πνευμονική αποκατάσταση
- Μεταμόσχευση πνευμόνων

Οξεία παρόξυνση IPF

- Συχνά πυροδοτείται από ένα οξύ συμβάν
- Μειοψηφία δεν αναγνωρίζεται αιτία (πρόοδος νόσου)

- ✓ Οξυγονοθεραπεία (NIV, HFNC)
- ✓ Μηχανικός αερισμός (μεταμόσχευση)
- ✓ Αντιμετώπιση αιτιολογικού παράγοντα
- ✓ Κορτικοστεροειδή;;

Acute exacerbation of idiopathic pulmonary fibrosis: international survey and call for harmonisation

Michael Kreuter[1,2,36], Markus Polke[1,36], Simon L.F. Walsh[3], Johannes Krisam[4], Harold R. Collard[5], Nazia Chaudhuri[6], Sergey Avdeev[7], Jürgen Behr[8,9], Gregory Calligaro[10], Tamera Corte[11], Kevin Flaherty[12], Manuela Funke-Chambour[13], Martin Kolb[14], Yasuhiro Kondoh[15], Toby M. Maher[16,17], Maria Molina Molina[18,19], Antonio Morais[20], Catharina C. Moor[21], Julie Morisset[22], Carlos Pereira[23], Silvia Quadrelli[24,25], Moises Selman[26], Argyrios Tzouvelekis[27], Claudia Valenzuela[28], Carlo Vancheri[29], Vanesa Vicens-Zygmunt[30,31], Julia Wälscher[1], Wim Wuyts[32], Marlies Wijsenbeek[21,37], Vincent Cottin[33,34,37] and Elisabeth Bendstrup[35,37]

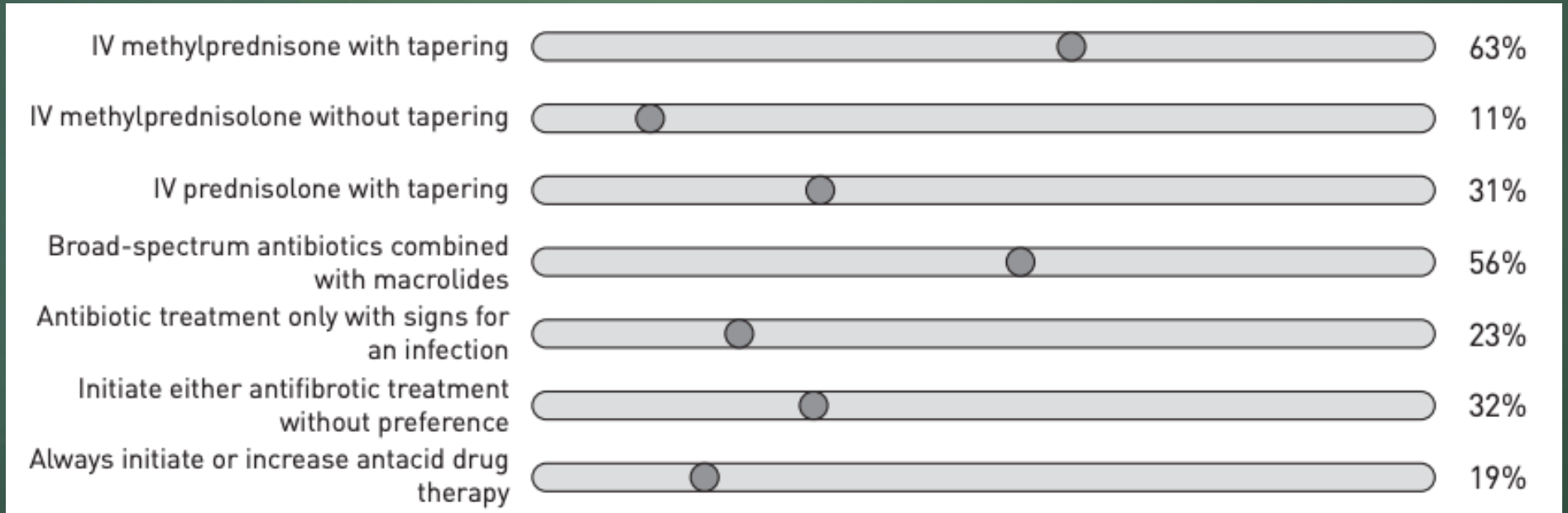
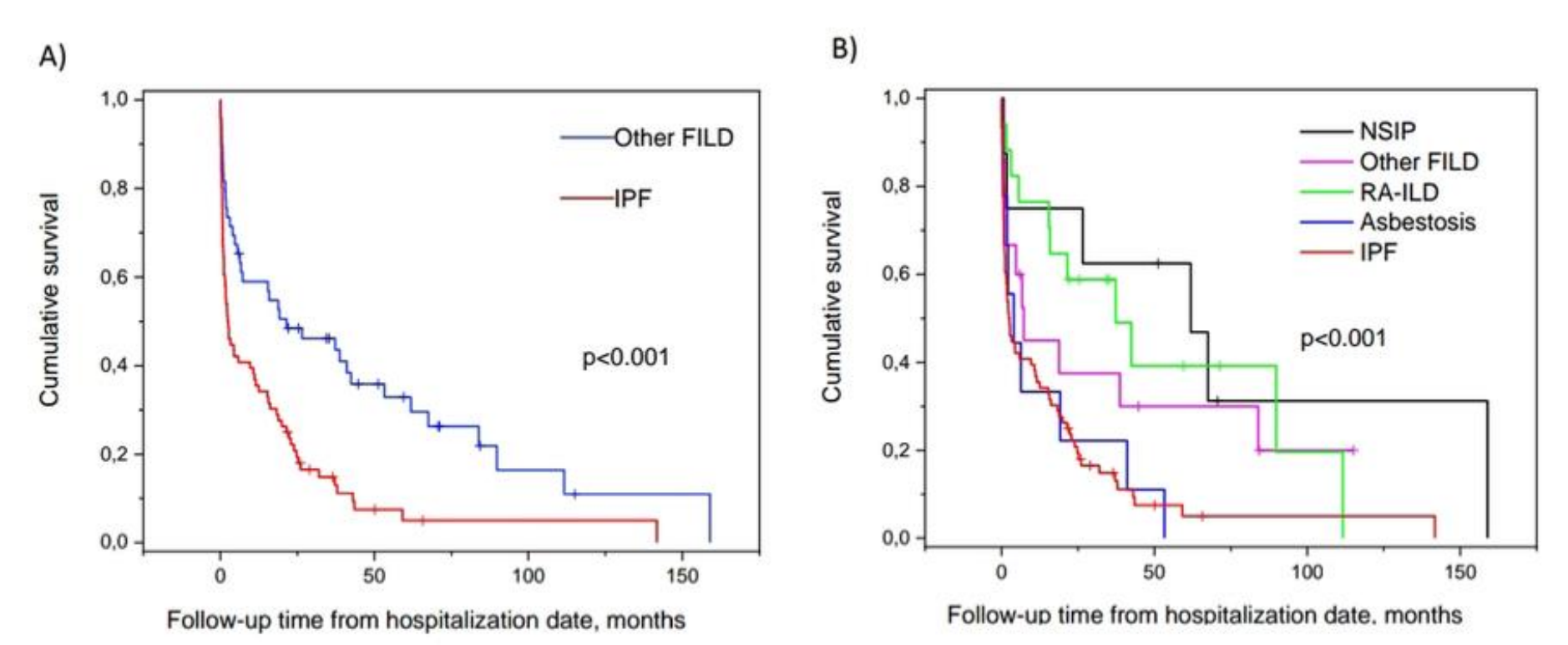


FIGURE 3 Main drug management approaches worldwide.

Prognosis and causes of death of patients with acute exacerbation of fibrosing interstitial lung diseases

Johanna Salonen ,[1,2] Minna Purokivi,[3] Risto Bloigu,[4] Riitta Kaarteenaho[1,2]



Συμπεράσματα

- Στόχος η επιβράδυνση της νόσου – επιβράδυνση της έκπτωσης της αναπνευστικής λειτουργίας
- Μείωση των παροξύνσεων
- Αύξηση της επιβίωσης
- Ποιότητα ζωής

Σας ευχαριστώ για την προσοχή σας